09-J4000-66

Original Effective Date: 01/01/24

Reviewed: 10/09/24

Revised: 11/15/24

Subject: Palovarotene (Sohonos) Oral Capsules

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Fibrodysplasia ossificans progressive (FOP) is a rare, genetic connective tissue disorder characterized by severe, progressive development of heterotopic ossification (HO), which is extraskeletal bone growth in muscle and soft tissue. The prevalence of FOP is approximately 1 in 1 million worldwide and is estimated to impact about 400 patients in the United States. FOP is caused by mutations in the activin A receptor type 1 gene (ACVR1), which encodes a bone morphogenetic protein (BMP) type I receptor that is important during the formation of the skeleton in the embryo and the repair of the skeleton following birth. The mutation in the ACVR1 gene increases BMP signaling, which results in the formation of heterotopic bone. Most cases of FOP occur sporadically; however, there are a few cases of inherited FOP in an autosomal dominant pattern. A hallmark clinical feature of FOP is the congenital bilateral great toe deformity at birth. Clinical presentation typically occurs within the first decade of life with episodes of painful soft tissue swelling, known as flare-ups, which are often precipitated by soft tissue injury, intramuscular injections, viral infections, or falls. These flare-ups lead to extraskeletal HO, which progresses throughout life. Classic FOP is characterized by bilateral hallux valgus malformations and early-onset, progressive HO while atypical FOP involves unilateral or lesser severity of hallux valgus malformations and later onset of HO. Eventually, HO leads to stiffness in affected areas, limited movement, and eventual fusion of affected joints and subsequent reduced mobility and activities of daily living. Most patients with FOP are confined to a wheelchair by their 30s with a median life expectancy of 56 years; death results from cardiorespiratory failure due to severe chest wall restriction.

Management strategies for patient with FOP is avoidance of non-emergent medical and dental procedures, falls, and activities that can cause flare-ups and potential HO. Historically, flare-ups have been treated with systemic corticosteroids with or without nonsteroidal anti-inflammatory medications. Additional second-line treatment options include leukotriene inhibitors, mast-cell stabilizers, imatinib, and bisphosphonates. On August 16, 2023, the FDA approved palovarotene (Sohonos) for reducing the

volume of new heterotopic ossification in adults and children aged 8 years and older for females and 10 years and older for males with FOP. Palovarotene (Sohonos) is an orally bioavailable retinoic acid receptor (RAR) agonist, with particular selectivity at the gamma subtype of RAR. Through binding to RARγ, palovarotene decreases BMP signaling, which reduces chondrogenesis and osteocyte differentiation resulting in reduced endochondral bone formation.

The safety and efficacy of palovarotene (Sohonos) was evaluated in two clinical trials. The first study was a phase 2, multicenter, randomized, double-blind, placebo-controlled, dose-ranging trial evaluating palovarotene for the prevention of HO in patients with FOP. Enrolled patients were greater than or equal to 6 years of age, diagnosed with classic FOP, had flare-up onset within 7 days prior to randomization, and were receiving current standard of care. Flare-ups were defined by the presence of two or more symptoms of pain, soft tissue swelling, decreased range of motion, stiffness, redness, or warmth. Patients of child-bearing potential were required to agree to remain abstinent or to use two highly effective forms of birth control, and pregnancy testing was performed before and during treatment. Patients were enrolled in two age-cohorts: (1) Age ≥ 15 years were randomized 3:1 to (a) palovarotene 10 mg daily for weeks 1 through 2 and 5 mg daily for weeks 3 through 6 or (b) placebo and (2) Age ≥ 6 years were randomized 3:3:2 to (a) palovarotene 10 mg daily for weeks 1 through 2 and 5 mg daily for weeks 3 through 6, (b) palovarotene 5 mg daily for weeks 1 through 2 and 2.5 mg daily for weeks 3 through 6 or (c) placebo. The primary endpoint was the proportion of responders (i.e., no/minimal new HO at flare-ups) at 6 weeks. Secondary endpoints included change from baseline in HO volume and new HO incidence assessed by computed tomography (CT) at week 12. Results from the two cohorts were pooled for analysis. Forty patients (aged 7 to 53 years) were enrolled and 39 were evaluated for per-protocol analysis (placebo: n = 10; palovarotene 5 mg-2.5 mg: n = 9; palovarotene 10 mg-5 mg: n = 20). At 6 weeks, proportion of responders was 100% in the palovarotene 10 mg-5 mg group, 88.9% in the palovarotene 5 mg-2.5 mg group, and 88.9% in the placebo group (p=0.17). At 12 weeks, the proportion of responders was 95% in the palovarotene 10 mg-5 mg group, 88.9% in the palovarotene 5 mg-2.5 mg group, and 77.8% in the placebo group (p=0.15). Additionally, at 12 weeks, the least-squares mean volume of new HO among all patients was 92.7% lower with palovarotene 5 mg-2.5 mg versus placebo and 79.0% lower with palovarotene 10 mg-5 mg versus placebo (p = 0.12 and p = 0.11, respectively). All patients reported at least one treatment-emergent adverse event (AE), with four reporting a serious AE, but none led to treatment discontinuation. AEs were consistent with those associated with retinoids (e.g., dry skin, dry lips, pruritus).

The second study evaluating palovarotene (Sohonos) was a phase 3, single-arm, open-label trial (MOVE trial). Enrolled FOP patients were 4 years of age and older and received palovarotene once daily based on the following regimens: weight-adjusted dosing regimen if skeletally immature or 5 mg (maintenance) and 20 mg for 4 weeks, then 10 mg for equal to or greater than 8 weeks (flare-up dosage). Exclusion criteria included those weighing less than 10 kg, concurrent tetracycline (or derivatives), vitamin A, beta carotene, strong inhibitors or inducers of cytochrome P450 3A4, or kinase inhibitors (e.g., imatinib), and those treated with synthetic oral retinoids within 4 weeks prior to screening. The primary study endpoint was annualized change in new HO volume as assessed by CT (excluding the head) compared with results from a FOP natural history study (NHS; NCT02322255), which was a prospective, longitudinal, 36-month study with patients receiving standard of care. A secondary endpoint included the proportion of patients with any new HO. There were 99 patients enrolled in the MOVE trial, with 97 being evaluated for comparison to the 101 patients in the FOP NHS.

At 12 months, there was no significant difference in the primary endpoint of annualized new HO, and the 12-month secondary endpoints showed no difference in the proportion of patients with any new HO (64% for palovarotene and 62% for FOP NHS) and in the mean number of body regions with new HO since baseline. However, an 18-month post hoc analyses, demonstrated the mean annualized new HO volume was 9.4 cm^3/year in patients receiving palovarotene and 20.3 cm^3/year in the FOP NHS population based on a linear mixed effect model. Therefore, the treatment effect was about 10.9 cm^3/year (95% CI: −21.2 cm^3/year, −0.6 cm^3/year). Additionally, the mean annualized new HO volume was 54% lower in MOVE trial versus the FOP NHS. All patients in MOVE reported at least one treatment-emergent adverse event (AE) with the most common AEs being dry skin (68.7%), lip dryness (46.5%), alopecia (34.3%), drug eruption(28.3%), and pruritus (26.3%) and musculoskeletal events such as arthralgia (33.3%), and partial or complete premature epiphyseal fusion or epiphyseal disorder AEs were observed in 21/57 (36.8%) patients who were less than 14 years of age.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of palovarotene (Sohonos) **meets the definition of medical necessity** when **ALL** of the following are met:

1. Diagnosis of fibrodysplasia ossificans progressive (FOP) as confirmed by the following (a and b): – Documentation must be submitted
    a. Identification of a heterozygous pathogenic variant in the ACVR1 gene
    b. Clinical symptoms (e.g., painful, recurrent soft-tissue swellings indicating flare-ups) and x-ray/CT imaging findings (e.g., bilateral or unilateral hallux valgus malformations) consistent with heterotopic ossification
2. Age of 8 years and older (females) or 10 years and older (males)
3. Negative pregnancy test prior to therapy initiation (only for women of reproductive potential)
4. Attestation that baseline x-rays (i.e., hand/wrist and knee), standard growth curves, and pubertal staging have been obtained prior to therapy initiation (only for members who have not reached skeletal maturity)
5. Member does not have moderate (Child-Pugh B) or severe hepatic impairment (Child-Pugh C)
6. The medication will not be prescribed concomitantly with strong CYP3A4 inhibitors (e.g., grapefruit/pomelo juice, fluconazole, itraconazole), strong and moderate CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort), vitamin A, or tetracyclines.
7. Prescribed by a specialist with expertise in the diagnosis and management of FOP such as an endocrinologist, rheumatologist, geneticist or orthopedic specialist.
8. The dose does not exceed the following (a or b)

a. Aged 14 years of age and older: 5 mg per day (maintenance) or 20 mg per day (flare-up)
b. Aged 8 to 13 years (females) and 10 to 13 years (males)
    i. Weight 10 kg to 19.9 kg: 2.5 mg per day (maintenance) or 10 mg per day (flare-up)
    ii. Weight 20 kg to 39.9 kg: 3 mg per day (maintenance) or 12.5 mg per day (flare-up)
    iii. Weight 40 kg to 59.9 kg: 4 mg per day (maintenance) or 15 mg per day (flare-up)
    iv. Weight equal to or greater than 60 kg: 5 mg per day (maintenance) or 20 mg per day (flare-up)

Approval duration: 6 months

Continuation of palovarotene (Sohonos) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization for the requested agent has been previously approved by Florida Blue or another health plan in the past 2 years (if another health plan, documentation of a health plan-paid claim during the 90 days before the authorization request must be submitted), **OR** the member has previously met all indication-specific initiation criteria.
2. Member has experienced a clinically beneficial response (e.g., stabilization or slowed heterotopic ossification, reduced flare-ups) from palovarotene (Sohonos) therapy without any clinically significant adverse effects (e.g., premature epiphyseal closure, spinal fractures, severe psychiatric symptoms, night blindness) necessitating discontinuation of therapy.
3. Recent negative pregnancy test (only for women of reproductive potential)
4. Member does not have moderate (Child-Pugh B) or severe hepatic impairment (Child-Pugh C)
5. The medication will not be prescribed concomitantly with strong CYP3A4 inhibitors (e.g., grapefruit/pomelo juice, fluconazole, itraconazole), strong and moderate CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort), vitamin A, or tetracyclines.
6. Prescribed by a specialist with expertise in the diagnosis and management of FOP such as an endocrinologist, rheumatologist, geneticist or orthopedic specialist.
7. The dose does not exceed the following (a or b)
    a. Aged 14 years of age and older: 5 mg per day (maintenance) or 20 mg per day (flare-up)
    b. Aged 8 to 13 years (females) and 10 to 13 years (males)
        i. Weight 10 kg to 19.9 kg: 2.5 mg per day (maintenance) or 10 mg per day (flare-up)
        ii. Weight 20 kg to 39.9 kg: 3 mg per day (maintenance) or 12.5 mg per day (flare-up)
        iii. Weight 40 kg to 59.9 kg: 4 mg per day (maintenance) or 15 mg per day (flare-up)
        iv. Weight equal to or greater than 60 kg: 5 mg per day (maintenance) or 20 mg per day (flare-up)

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Palovarotene (Sohonos) is a retinoid indicated for reduction in the volume of new heterotopic ossification in adults and children aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressive (FOP).
- The recommended dosage for adults and pediatric patients 14 years of age and older is 5 mg daily. Patients may experience flare-up symptoms requiring higher doses as follows:
    - The recommended flare-up dosage for adults and pediatric patients 14 years and older is 20 mg daily for 4 weeks, followed by 10 mg daily for 8 weeks (for a total of 12 weeks of flare-up treatment), even if symptoms resolve earlier, then return to daily dosing of 5 mg.
    - If during the course of flare-up treatment, the patient experiences marked worsening of the original flare-up site or another flare-up at a new location, restart the 12-week flare-up dosing at 20 mg daily.
    - For flare-up symptoms that have not resolved at the end of the 12-week period, the 10 mg daily dosage may be extended in 4-week intervals and continued until the flare-up symptoms resolve. If new flare-up symptoms occur after the 5 mg daily dosing is resumed, flare-up dosing may be restarted.
- The recommended daily and flare-up dosages for pediatric patients aged 8 to 13 years for females and aged 10 to 13 years for males are weight-based and are provided in Table 1. Administer the initial flare-up dosage once daily for 4 weeks, then administer the lower flare-up dosage once daily for 8 weeks (for a total of 12 weeks of flare-up treatment), even if symptoms resolve earlier, then return to daily dosing.
    - If during the course of flare-up treatment, the patient experiences marked worsening of the original flare-up site or another flare-up at a new location, restart the 12-week flare-up dosing with the Week 1 to 4 dose.
    - For flare-up symptoms that have not resolved at the end of the 12-week period, the Week 5 to 12 flare-up dose may be extended in 4-week intervals and continued until the flare-up symptoms resolve. If new flare-up symptoms occur after daily dosing is resumed, flare-up dosing may be restarted.

Table 1. Recommended Palovarotene (Sohonos) Weight-Based Dosage for Pediatric Patients Aged 8 to 13 Years for Females and 10 to 13 Years for Males*

Weight	Daily Dosage	Week 1 to 4 Flare-up Dosage	Week 5 to 12 Flare-up Dosage
10 kg to 19.9 kg	2.5 mg	10 mg	5 mg
20 kg to 39.9 kg	3 mg	12.5 mg	6 mg
40 kg to 59.9 kg	4 mg	15 mg	7.5 mg

≥ 60 kg	5 mg	20 mg	10 mg

*Once daily

- The daily dosing regimen should be stopped when flare-up dosing begins. Additionally, initiate flare-up treatment at the onset of the first symptom indicative of a FOP flare-up or substantial high-risk traumatic event likely to lead to a flare-up (e.g., surgery, intramuscular immunization, mandibular blocks for dental procedures, muscle fatigue, blunt muscle trauma from bumps, bruises, falls, or influenza-like viral illnesses). Symptoms of a FOP flare-up typically include but are not limited to localized pain, soft tissue swelling/inflammation, redness, warmth, decreased joint range of motion, and stiffness.
- It is recommended to take palovarotene (Sohonos) with food preferably at the same time each day. The capsules may be swallowed whole or may be opened and the contents emptied onto one teaspoon (5 mL) of soft food (e.g., apple sauce, low-fat yogurt, or warm oatmeal) and taken within 1 hour of opening, provided it was maintained at room temperature and not exposed to direct sunlight. Do not administer palovarotene (Sohonos) with grapefruit, pomelo, or juices containing these fruits.

Dose Adjustments

- Patients may experience adverse reactions to palovarotene (Sohonos) that require dosage reduction during either the daily dosing or flare-up dosing. The recommended reduction is to reduce the daily dosage to the next lower dose as shown in Table 2 at the discretion of the healthcare provider. Doses may be reduced further if the adverse reactions do not improve. If the patient is already receiving the lowest possible tolerated dose, then consider discontinuing the medication temporarily or permanently. Initiate subsequent flare-up dosing at the same reduced dose that was tolerated previously.

Table 2. Dose Reduction of Palovarotene (Sohonos) for Flare-Up and Chronic Treatment

Dose Prescribed	Reduced Dose
20 mg	15 mg
15 mg	12.5 mg
12.5 mg	10 mg
10 mg	7.5 mg
7.5 mg	5 mg
6 mg	4 mg
5 mg	2.5 mg
4 mg	2 mg
3 mg	1.5 mg
2.5 mg	1 mg

- Palovarotene (Sohonos) undergoes extensive hepatic metabolism. No dose adjustment is recommended in patients with mild (Child-Pugh A) hepatic impairment; however, use in patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment is not recommended.

- CYP3A4 inhibitors may increase palovarotene (Sohonos) exposure, and CYP3A4 inducers may decrease exposure. Therefore, it is recommended to avoid concomitant use of CYP3A4 strong inhibitors (e.g., grapefruit/pomelo juice, fluconazole, itraconazole) as well as moderate and strong inducers of CYP3A4 (e.g., rifampin, carbamazepine, St. John's Wort).
- If concomitant use with moderate CYP3A inhibitors will occur, reduce the dose by half as shown in Table 3.

Table 3. Dose Reduction of Palovarotene (Sohonos) for Use with Moderate CYP3A Inhibitors

Weight	Daily Dosage	Week 1 to 4 Flare-up Dosage	Week 5 to 12 Flare-up Dosage
10 kg to 19.9 kg	1 mg	5 mg	2.5 mg
20 kg to 39.9 kg	1.5 mg	6 mg	3 mg
40 kg to 59.9 kg	2 mg	7.5 mg	4 mg
≥ 60 kg*	2.5 mg	10 mg	5 mg

*All pediatric patients ≥14 years of age and adults should receive the dose in the ≥60 kg weight category.

- Palovarotene (Sohonos) belongs to the same pharmacological class as vitamin A; therefore, these agents should not be prescribed concomitantly to avoid additive effects and the risk of hypervitaminosis A.
- Systemic retinoid use has been associated with cases of benign intracranial hypertension (i.e., pseudotumor cerebri), some of which involved the concomitant use of tetracyclines; therefore, palovarotene (Sohonos) should not be co-administered with tetracycline derivatives.

Drug Availability

- Palovarotene (Sohonos) capsules
  - 1 mg (NDC 15054-0010-1)
  - 1.5 mg (NDC 15054-0015-1)
  - 2.5 mg (NDC 15054-0025-1)
  - 5 mg (NDC 15054-0050-1)
  - 10 mg (NDC 15054-0100-1)
- Supplied as a blister strip containing 14 capsules in a child resistant carton

PRECAUTIONS:

Boxed Warning

- **Embryo-Fetal Toxicity:** Palovarotene (Sohonos) may cause fetal harm. Because of the risk of teratogenicity and to minimize fetal exposure, it is to be administered only if conditions for pregnancy prevention are met. For females of reproductive potential, obtain a negative pregnancy

test within one week prior to initiating and periodically during palovarotene (Sohonos) therapy. If pregnancy occurs, stop treatment immediately and refer the patient to an obstetrician/gynecologist experienced in reproductive toxicity. Additionally, advise females of reproductive potential to use effective contraception at least one month prior to treatment, during treatment, and for 1 month after the last dose, unless continuous abstinence is chosen.

- **Premature Epiphyseal Closure:** Premature epiphyseal closure occurred with palovarotene (Sohonos) therapy. Prior to starting treatment, all growing pediatric patients should undergo baseline assessment of skeletal maturity via hand/wrist and knee x-rays, standard growth curves and pubertal staging. Continued monitoring is recommended every 6 to 12 months until patients reach skeletal maturity or final adult height. If a patient exhibits signs of premature epiphyseal closure or adverse effects on growth based on clinical or radiologic evaluations, further evaluation may be required, including an assessment of the benefits and risks of continued treatment, or temporary or permanent discontinuation of palovarotene (Sohonos) until the patient achieves epiphyseal closure and skeletal maturity.

Contraindications

- Pregnancy
- A history of allergy or hypersensitivity (e.g., anaphylaxis) to retinoids, or to any component of palovarotene (Sohonos).

Precautions/Warnings

- **Mucocutaneous Adverse Reactions:** Dry skin, lip dry, pruritis, rash, alopecia, erythema, skin exfoliation, and dry eye may occur with palovarotene (Sohonos) therapy. Photosensitivity reactions, such as exaggerated sunburn reactions (e.g., burning, erythema, blistering) involving areas exposed to the sun have been associated with the use of retinoids and may occur with palovarotene (Sohonos). Precautionary measures for phototoxicity are recommended. Excessive exposure to sun or artificial ultraviolet light should be avoided, and protection from sunlight should be used when exposure cannot be avoided. To prevent or treat these reactions it is recommended to use skin emollients, sunscreen, and artificial tears. Dosage reduction may be required in some cases.
- **Metabolic Bone Disorders:** Retinoids are associated with bone toxicity, including reductions in bone mass and spontaneous reports of osteoporosis and fracture. In FOP clinical trials, palovarotene (Sohonos) resulted in decreased vertebral bone mineral content and bone density, and an increased risk of radiologically observed vertebral (T4 to L4) fractures in treated adult and pediatric patients compared to untreated patients. Periodic radiological assessment of the spine is recommended. Additionally, retinoids have been associated with hyperostotic changes (bone spurs) and calcification of tendons or ligaments and may occur with palovarotene (Sohonos). These effects generally occur with long-term use, especially at high doses.
- **Psychiatric Disorders**: New or worsening psychiatric events have been reported with palovarotene (Sohonos) use. These include depression, anxiety, mood alterations and suicidal thoughts and behaviors. There is a relatively high background prevalence of psychiatric disorders in untreated patients with FOP. Monitor for development of new or worsening psychiatric symptoms during treatment. Individuals with a history of psychiatric illness may be more susceptible to these adverse effects. Patients should be advised to contact their healthcare provider if new or worsening psychiatric symptoms develop during treatment.

- **Night Blindness:** Night blindness has been associated with systemic retinoids, including palovarotene (Sohonos). This may be dose-dependent, making driving a vehicle at night potentially hazardous during treatment. Night blindness is generally reversible after cessation of treatment but can also persist in some cases. Patients should be advised to be cautious when driving or operating any vehicle at night and to seek medical attention in the event of vision impairment.

BILLING/CODING INFORMATION:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, not otherwise specified

ICD-10 Diagnosis Codes That Support Medical Necessity

M61.10	Myositis ossificans progressiva, unspecified site
M61.111	Myositis ossificans progressiva, right shoulder
M61.112	Myositis ossificans progressiva, left shoulder
M61.119	Myositis ossificans progressiva, unspecified shoulder
M61.121	Myositis ossificans progressiva, right upper arm
M61.122	Myositis ossificans progressiva, left upper arm
M61.129	Myositis ossificans progressiva, unspecified arm
M61.131	Myositis ossificans progressiva, right forearm
M61.132	Myositis ossificans progressiva, left forearm
M61.139	Myositis ossificans progressiva, unspecified forearm
M61.141	Myositis ossificans progressiva, right hand
M61.142	Myositis ossificans progressiva, left hand
M61.143	Myositis ossificans progressiva, unspecified hand
M61.144	Myositis ossificans progressiva, right finger(s)
M61.145	Myositis ossificans progressiva, left finger(s)
M61.146	Myositis ossificans progressiva, unspecified finger(s)
M61.151	Myositis ossificans progressiva, right thigh
M61.152	Myositis ossificans progressiva, left thigh
M61.159	Myositis ossificans progressiva, unspecified thigh
M61.161	Myositis ossificans progressiva, right lower leg
M61.162	Myositis ossificans progressiva, left lower leg
M61.169	Myositis ossificans progressiva, unspecified lower leg
M61.171	Myositis ossificans progressiva, right ankle
M61.172	Myositis ossificans progressiva, left ankle
M61.173	Myositis ossificans progressiva, unspecified ankle
M61.174	Myositis ossificans progressiva, right foot
M61.175	Myositis ossificans progressiva, left foot
M61.176	Myositis ossificans progressiva, unspecified foot
M61.177	Myositis ossificans progressiva, right toe(s)
M61.178	Myositis ossificans progressiva, left toe(s)
M61.179	Myositis ossificans progressiva, unspecified toe(s)

M61.18	Myositis ossificans progressiva, other site
M61.19	Myositis ossificans progressiva, multiple sites

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2024. URL www.clinicalpharmacilogy-ip.com Accessed 9/24/24.
2. DynaMed [database online]. Ipswich, MA: EBSCO Information Services.; 2024. URL http://www.dynamed.com. Accessed 9/24/24.
3. Micromedex Healthcare Series [Internet Database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Accessed 9/24/24.
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 2024 Sept 24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
5. Pignolo RJ, Baujat G, Hsiao EC, et al. Palovarotene for Fibrodysplasia Ossificans Progressiva (FOP): Results of a Randomized, Placebo-Controlled, Double-Blind Phase 2 Trial. *J Bone Miner Res*. 2022;37(10):1891-1902. doi:10.1002/jbmr.4655

6. Pignolo RJ, Hsiao EC, Al Mukaddam M, et al. Reduction of New Heterotopic Ossification (HO) in the Open-Label, Phase 3 MOVE Trial of Palovarotene for Fibrodysplasia Ossificans Progressiva (FOP). *J Bone Miner Res*. 2023;38(3):381-394. doi:10.1002/jbmr.4762
7. Sohonos (palovarotene) oral capsules [package insert]: Ipsen Biopharmaceuticals, Inc., Cambridge (MA): August 2023.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/09/24.

GUIDELINE UPDATE INFORMATION:

01/01/24	New Medical Coverage Guideline – Palovarotene (Sohonos) for reduction of new heterotopic ossification in patients with fibrodysplasia ossificans progressive.
11/15/24	Review and revision to the guideline consisting of revising the position statement to avoid use in patients with moderate hepatic impairment (Child-Pugh B) and updated references.